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Lectura recomendada

Synthesis and evaluation of a novel ^{68}Ga-chelate-conjugated bisphosphonate as a bone-seeking agent for PET imaging

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Introduction: ^{68}Ga is a positron-emitting nuclide that has significant imaging potential given that, unlike cyclotron-produced ^{18}F, the isotope can be produced on-site utilizing a ^{68}Ge/^{68}Ga generator. We recently synthesized a novel bone-seeking agent by coupling a bisphosphonate with the ^{68}Ga chelator 1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA). This study presents a first report on the potential of this ^{68}Ga bone-seeking radiopharmaceutical in the detection of bone metastases.

Methods: 4-Amino-1-hydroxybutylidene-1,1-bisphosphonate was conjugated with 2-[4,7-di(carboxymethyl)-1,4,7-triazonan-1-yl]pentanedioic acid, yielding 2-[4,7-di(carboxymethyl)-1,4,7-triazonan-1-yl]-5-[(4-hydroxy-4,4-diphosphonobutyl)amino]-5-oxopentanoic acid (NOTA-BP). ^{68}Ga-labeled NOTA-BP ([^{68}Ga]NOTA-BP) was prepared by complexation of NOTA-BP with [^{68}Ga] gallium chloride and evaluated in in vitro experiments, biodistribution experiments and micro-positron emission tomography (PET) imaging experiments.

Results: The labeling of NOTA-BP with ^{68}Ga was completed by heating for 10 min. [^{68}Ga]NOTA-BP was determined to have a radiochemical purity of over 95%, a high affinity for hydroxyapatite and a high stability in plasma. In in vivo biodistribution experiments, [^{68}Ga]NOTA-BP demonstrated high bone uptake potential. Compared with ^{99m}Tc-labeled methylene diphosphonate ([^{99m}Tc]MDP) and [^{18}F]fluoride, [^{68}Ga]NOTA-BP exhibited faster blood clearance and a higher bone-to-blood ratio. In addition, mouse model bone metastasis was detected by micro-PET imaging at 1 h postinjection of [^{68}Ga]NOTA-BP.

Conclusion: We have developed a novel ^{68}Ga-radiolabeled bone-seeking agent. This [^{68}Ga]NOTA-BP complex was found to have a high bone affinity and rapid blood clearance, and may thus prove to be useful as a bone-seeking agent for clinical PET.

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